This report is required by law (7 USC 2143). Failure to report according to the regulations can result in an order to cease and desist and to be subject to penalties as provided for in Section 2150.

See reverse side for additional information.

Interagency Report Control No
0180-DOA-AN

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

ANNUAL REPORT OF RESEARCH FACILITY

(TYPE OR PRINT)

1. REGISTRATION NO. 55-R-0001

CUSTOMER NO. 825

FORM APPROVED
OMB NO. 0579-0036

2. HEADQUARTERS RESEARCH FACILITY *(Name and Address, as registered with USDA, include Zip Code)*

WAKE FOREST UNIVERSITY
MEDICAL CENTER BOULEVARD
WINSTON SALEM, NC 27109

3. REPORTING FACILITY (List all locations where animals were housed or used in actual research, testing, teaching, or experimentation, or held for these purposes. Attach additional sheets if necessary.)

FACILITY LOCATIONS*(sites)*

(b)(2)High, (b)(7)f

REPORT OF ANIMALS USED BY OR UNDER CONTROL OF RESEARCH FACILITY *(Attach additional sheets if necessary or use APHIS FORM 7023A)*

A. Animals Covered By The Animal Welfare Regulations	B. Number of animals being bred, conditioned, or held for use in teaching, testing, experiments, research, or surgery but not yet used for such purposes.	C. Number of animals upon which teaching, research, experiments, or tests were conducted involving no pain, distress, or use of pain-relieving drugs.	D. Number of animals upon which experiments, teaching, research, surgery, or tests were conducted involving accompanying pain or distress to the animals and for which appropriate anesthetic, analgesic, or tranquilizing drugs were used.	E. Number of animals upon which teaching, experiments, research, surgery or tests were conducted involving accompanying pain or distress to the animals and for which the use of appropriate anesthetic,analgesic, or tranquilizing drugs would have adversely affected the procedures, results, or interpretation of the teaching, research, experiments, surgery, or tests. *(An explanation of the procedures producing pain or distress in these animals and the reasons such drugs were not used must be attached to this report)*	F. TOTAL NO. OF ANIMALS **(Cols. C + D + E)**
4. Dogs			58		58
5. Cats			78		78
6. Guinea Pigs					
7. Hamsters					
8. Rabbits			204		204
9. Non-Human Primates		181	716	17	914
10. Sheep			224		224
11. Pigs			74		74
12. Other Farm Animals					
13. Other Animals					
Bats		5			5
Squirrels		60			60
Ferrets		112	6		118

ASSURANCE STATEMENTS

1) Professionally acceptable standards governing the care, treatment, and use of animals, including appropriate use of anesthetic, analgesic, and tranquilizing drugs, prior to, during, and following actual research, teaching, testing, surgery, or experimentation were followed by this research facility.
2) Each principal investigator has considered alternatives to painful procedures.
3) This facility is adhering to the standards and regulations under the Act, and it has required that exceptions to the standards and regulations be specified and explained by the principal investigator and approved by the Institutional Animal Care and Use Committee (IACUC). **A summary of all the exceptions is attached to this annual report.** In addition to identifying the IACUC-approved exceptions, this summary includes a brief explanation of the exceptions, as well as the species and number of animals affected.
4) The attending veterinarian for this research facility has appropriate authority to ensure the provision of adequate veterinary care and to oversee the adequacy of other aspects of animal care and use.

CERTIFICATION BY HEADQUARTERS RESEARCH FACILITY OFFICIAL

(Chief Executive Officer or Legally Responsible Institutional official)

I certify that the above is true, correct, and complete (7 U.S.C. Section 2143)

SIGNATURE OF C.E.O. OR INSTITUTIONAL OFFICIAL	NAME & TITLE OF C.E.O. OR INSTITUTIONAL OFFICIAL *(Type or Print)*	DATE SIGNED
(b)(6), (b)(7)c		11/02/2007

APHIS FORM 7023
(AUG 91)

(Replaces VS FORM 18-23 (Oct 88), which is obsolete

PART 1 - HEADQUARTERS

This report is required by law (7 USC 2143). Failure to report according to the regulations can result in an order to cease and desist and to be subject to penalties as provided for in Section 2150.

See reverse side for additional information.

Interagency Report Control No
0180-DOA-AN

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

CONTINUATION SHEET FOR ANNUAL REPORT OF RESEARCH FACILITY

(TYPE OR PRINT)

1. REGISTRATION NO. 55-R-0001

CUSTOMER NO. 825

FORM APPROVED
OMB NO. 0579-0036

2. HEADQUARTERS RESEARCH FACILITY *(Name and Address, as registered with USDA, include Zip Code)*

WAKE FOREST UNIVERSITY
MEDICAL CENTER BOULEVARD
WINSTON SALEM, NC 27109

REPORT OF ANIMALS USED BY OR UNDER CONTROL OF RESEARCH FACILITY *(Attach additional sheets if necessary or use this form.)*

A. Animals Covered By The Animal Welfare Regulations	B. Number of animals being bred, conditioned, or held for use in teaching, testing, experiments, research, or surgery but not yet used for such purposes.	C. Number of animals upon which teaching, research, experiments, or tests were conducted involving no pain, distress, or use of pain-relieving drugs.	D. Number of animals upon which experiments, teaching, research, surgery, or tests were conducted involving accompanying pain or distress to the animals and for which appropriate anesthetic, analgesic, or tranquilizing drugs were used.	E. Number of animals upon which teaching, experiments, research, surgery or tests were conducted involving accompanying pain or distress to the animals and for which the use of appropriate anesthetic,analgesic, or tranquilizing drugs would have adversely affected the procedures, results, or interpretation of the teaching, research, experiments, surgery, or tests. *(An explanation of the procedures producing pain or distress in these animals and the reasons such drugs were not used must be attached to this report)*	F. TOTAL NO. OF ANIMALS **(Cols. C + D + E)**
Chinchillas			155		155

ASSURANCE STATEMENTS

1) Professionally acceptable standards governing the care, treatment, and use of animals, including appropriate use of anesthetic, analgesic, and tranquilizing drugs, prior to, during, and following actual research, teaching, testing, surgery, or experimentation were followed by this research facility.
2) Each principal investigator has considered alternatives to painful procedures.
3) This facility is adhering to the standards and regulations under the Act, and it has required that exceptions to the standards and regulations be specified and explained by the principal investigator and approved by the Institutional Animal Care and Use Committee (IACUC). **A summary of all the exceptions is attached to this annual report.** In addition to identifying the IACUC-approved exceptions, this summary includes a brief explanation of the exceptions, as well as the species and number of animals affected.
4) The attending veterinarian for this research facility has appropriate authority to ensure the provision of adequate veterinary care and to oversee the adequacy of other aspects of animal care and use.

CERTIFICATION BY HEADQUARTERS RESEARCH FACILITY OFFICIAL
(Chief Executive Officer or Legally Responsible Institutional official)

I certify that the above is true, correct, and complete (7 U.S.C. Section 2143)

SIGNATURE OF C.E.O. OR INSTITUTIONAL OFFICIAL	NAME & TITLE OF C.E.O. OR INSTITUTIONAL OFFICIAL *(Type or Print)*	DATE SIGNED
(b)(6), (b)(7)c		11/02/2007

APHIS FORM 7023A
(AUG 91)

(Replaces VS FORM 18-23 (Oct 88), which is obsolete

PART 1 - HEADQUARTERS

APHIS Form 7023 Column E Explanation

This form is intended as an aid to completing the APHIS Form 7023 Column E explanation. It is not an official form and its use is voluntary. Names, addresses, protocols, veterinary care programs, and the like, are not required as part of an explanation. A Column E explanation must be written so as to be understood by lay persons as well as scientists.

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1. Registration Number: 55-R-0001

2/3. Species (common name) & Number of animals used in this study:

Non-Human Primates (17)

4. Explain the procedure producing pain and/or distress.

One of the aims of this study is to identify those brain areas most affected by sleep deprivation in an animal model. To that end, monkeys are kept awake for 36-54 hours by use of nonaversive stimuli (lights, videos, music, food treats, toys, random computer sounds, interactions with technicians). Behavioral, electrophysiological, and brain metabolic parameters measured after deprivation are compared to baseline parameters. Sleep deprivation studies are performed at minimum 10 day intervals, typically only once per 2-4 weeks per monkey. While the procedures used to produce sleep deprivation are not themselves considered painful, it is recognized that the lack of sleep may cause monkeys to experience some unrelieved distress during the 36-54 hours when they are kept awake. However, such distress is not entirely unrelieved, since the monkeys are allowed to sleep once the physiological and behavioral assessments are completed. In addition, sleep deprivation procedures utilize nonaversive alerting stimuli, constant interaction with technician staff with whom the monkeys are most familiar, and maintainance of social interaction by working with two or more monkeys at a time. Upon completion of the procedure, the monkeys are returned to their home cage and normal social environment and allowed to sleep. They are also given a normal 12 hour sleep cycle that night.

5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results. (For Federally mandated testing, see Item 6 below)

Although humans can undergo brief periods with little to no sleep, the problems of extended sleep deprivation are vitally important especially for military personnel, shift-workers, medical personnel, mothers with very young children, and long-distance truck drivers, all of whom must continue to do their essential duties with prolonged periods of sleep loss or interruption. Despite such sleep deprivation, societal and job demands require these individuals to be attentive, remember accurately, and make appropriate decisions. Before an effective means of alleviating the effects of sleep deprivation on memory, attention, and decision-making can be developed, it is necessary to identify those cognitive functions and brain areas most affected by sleep deprivation. This ACUC approved study is necessary to characterize the effects of sleep deprivation in an animal model that is quite similar to that of a human performing a job that requires hand-eye coordination, short-term memory, and decisions based on information presented in the task. The experiment provides access to information (i.e. electrophysiological measures and testing of paliative drugs) that cannot be obtained in human studies. The procedures themselves are not painful, but the actual experience of being sleep-deprived may result in distress to the monkeys, which would be unrelieved during the 36-54 hours that they are kept awake. However, since the stress of sleep deprivation is precisely the effect being studied, it cannot be alleviated during the period of the experiment. Efforts are made to alleviate the distress as soon as the experimental measurements are completed, and sleep deprivation is not repeated for a minimum of 10 days.

6. What, if any, federal regulations require this procedure? Cite the agency, the code of Federal Regulations (CFR) title number and the specific section number (e.g., APHIS, 9 CFR 113.102):

Agency: Agency: CFR: CFR:

Attachment to APHIS FORM 7023

Summary of Exceptions to Regulations and Standards
Wake Forest University 55-R-0001
Fiscal Year 2006-2007

1. The following is an exception to the requirements for sanitizing nonhuman primate primary enclosures at required frequencies:

(b)(2)High, (b)(7)f is used to house nonhuman primates imported directly from foreign sources (Indonesia). As recommended by the Centers for Disease Control (CDC), cages used in this building are not sent through the mechanical cage washer until after the first thirty-one days (Phase I) of quarantine to reduce the transmission of possible infectious agents . Animal waste is removed from cage pans daily. After monkeys have completed Phase I quarantine, cages are sanitized at intervals in accordance with federal regulations and standards.

2. All of the following protocols involve exceptions to the cage size requirements for sheep primary enclosures. Each exception was approved by the Wake Forest University (WFU) Instituitional Animal Care and Use Committee (IACUC), after their determination of scientific justification. For each protocol listed, sheep *(Ovis aries)* are used in studies of pituitary-adrenal hormones, renin, and vasopressin, and are housed in metabolism carts for up to fourteen days. These studies are important to the understanding of factors relating to the health and survival of newborn infants. The Committee's justification for the exception is based on data that show movement of animals in and out of the carts on a daily basis would adversely influence the hormones measured in these experiments.

A06-003: Prenatal and Neonatal Pituitary-Adrenal Function	Number Used: 21
A05-075: Project 2: Antenatal Steroids Exposure and Renal Sodium Handling	Number Used: 20
A05-076: Project 1: The Impact of Antenatal Steroid Exposure on the Intrarenal REnin- Angiotensin System, Renal Function and Blood Pressure	Number Used: 21
A05-078: Project 3: Antenatal steroid exposure and neurogenic control of blood pressure	Number Used: 6
A05-105: Vulnerability of the Fetal Brain to Hypoxia-Ischemi	Number Used: 4

3. The following protocols involve exceptions to the requirements for watering nonhuman primates. For each protocol listed, full access to water is regulated in a manner to ensure animals are adequately motivated to perform traditional operant conditioning paradigms. Each exception was approved by the WFU IACUC, after their determination of scientific justification.

a. A06-122: Diencephalic Mechanisms of Visuomotor Integration
Access to water is regulated such that the first fluid intake of the day will occur during a training or experimental session. A well-trained animal will work to satiety during an experimental session and, in doing so, obtain its minimum daily water requirement. In the event that an animal does not obtain its minimum fluid intake during a session, fluid will be supplemented to the appropriate level when the animal is returned to its home cage. Typically, water regulation is begun on Sunday in preparation for behavioral testing on Monday. Animals participate in experiments on Monday through Friday and receive ad libitum access to water on Friday afternoon through Sunday morning. Throughout the duration of an individual animal's participation in experimental protocols, fluid intake, weight, and a variety of other physiological

and behavioral measures are recorded to assure the animal's continued health and well-being. Animals are weighed daily (on the days they are tested). Health and hydration are assessed every day by both research and veterinary personnel. These studies are important to understanding the neural bases of sensory and motor control of the mechanisms of decision making in humans.

Species Used: Male rhesus monkeys (*Macaca mulatta*)
Number Used: 5

b. *A04-050: Cortical Implications for Rehabilitation*
Access to water is regulated such that the first fluid intake of the day will occur during a training or experimental session. A well-trained animal will work to satiety during an experimental session and, in doing so, obtain its minimum daily water requirement. In the event that an animal does not obtain its minimum fluid intake during a session, fluid will be supplemented to the appropriate level when the animal is returned to its home cage. Typically, water regulation is begun on Sunday in preparation for behavioral testing on Monday. Animals participate in experiments on Monday through Friday and receive ad libitum access to water on Friday afternoon through Sunday morning. Throughout the duration of an individual animal's participation in experimental protocols, fluid intake, weight, and a variety of other physiological and behavioral measures are recorded to assure the animal's continued health and well-being. Animals are weighed daily (on the days they are tested). Health and hydration are assessed every day by both research and veterinary personnel. Findings from this study will aid in improving rehabilitive therapy for individuals following a stroke.

Species Used: Male rhesus monkeys (*Macaca mulatta*)
Number Used: 2

c. *Protocol A07-036 (replaced A05-165 on 5/1/07): Multisensory integration: Midbrain and Neocortex*

Water regulation only occurs during periods of training and experimentation.
At other times, animals are given ad lib access to water. Prior to beginning training, each animals' ad lib intake of fluid will be recorded to determine its normal daily consumption, usually in the range of 20-40 ml/kg. On training and experimental days, animals' water intake will be restricted, such as that their first fluid intake of the day will occur during a training or experimental session. Animals are expected to work to satiety, obtaining more than their minimum fluid requirement. In the event that an animal does not obtain its minimum intake during a session (particularly during the early stages of training) it will be supplemented after the end of the session by the investigator. Animals will participate in experiments 5 days a week and have free access to water for two days per week. The animals' appetite and hydration will be logged daily, and the animals' weight will be recorded at least twice per week (daily during experiments).
Additionally, animals' health will be monitored by daily observation by both research and veterinary staff. These studies will provide information about how the presence of one kind of environmental energy (e.g. sight) affects the perception of another kind of energy (e.g. sound), and the neural mechanisms that underlie these function.

Species Used: Male rhesus monkeys (*Macaca mulatta*)
Number Used: 3

d. *Protocol A07-037: Subcortical neural basis of hearing in primates*

Water regulation only occurs during periods of training and experimentation.
At other times, animals are given ad lib access to water. Prior to beginning training, each animals' ad lib intake of fluid will be recorded to determine its normal daily consumption, usually in the range of 20-40 ml/kg. On training and experimental days, animals' water intake will be restricted, such as that their first fluid intake of the day will occur during a training or experimental session. Animals are expected to work to satiety, obtaining more than their minimum fluid requirement. In the event that an animal does not obtain its minimum intake during a session (particularly during the early stages of training) it will be supplemented after the end of the session by the investigator. Animals will participate in experiments 5 days a week and have free access to water for two days per week. The animals' appetite and hydration will be logged daily, and the animals[1] weight will be recorded at least twice per week (daily during experiments).
Additionally, animals' health will be monitored by daily observation by both research and veterinary staff. These studies will provide information about how behavior is influenced by various properties of sound, and how neurons responsive to sound contribute to those particular behaviors.

Species Used: Male rhesus monkeys (*Macaca mulatta*)
Number Used: 2

e. *A06-034/A07-127: The Cortical Circuitry that Mediates Working Memory*
Water intake is regulated so that the animals' first fluid intake of the day occurs during a training or experimental session. Fully-trained animals work to satiety, obtaining more than their minimum fluid requirement. In the event that an animal does not obtain its minimum intake during a session (particularly during the early stages of training) it is supplemented after the end of the session by the investigator. Animals participate in experiments 5 days a week and have free access to water for two days per week. Prior to beginning training, each animal's ad lib intake of fluid is recorded to determine its normal daily consumption. This is generally in the range of 20-40 ml/kg. A daily record is made of the animal's fluid and food intake. Body weights are recorded at least twice per week (daily during experiments). Health and hydration are assessed every day by both research and veterinary personnel. Water regulation is temporarily suspended if a monkey exhibits signs of dehydration (i.e. decreased urine production, dry feces, anorexia, changes in skin elasticity). Findings from this project will offer insight into possible means of reversing the effects in humans of brain damage and mental illness.

Species Used: Male rhesus monkeys (*Macaca mulatta*)
Number Used: 3

f. *A06-033: Distributed, Passive, and Active Components of Memory*
Water intake is regulated so that the animals' first fluid intake of the day occurs during a training or experimental session. Fully-trained animals work to satiety, obtaining more than their minimum fluid requirement. In the event that an animal does not obtain its minimum intake during a session (particularly during the early stages of training) it is supplemented after the end of the session by the investigator. Animals participate in experiments 5 days a week and have free access to water for two days per week. Prior to beginning training, each animal's ad lib intake of fluid is recorded to determine its normal daily consumption. This is generally in the range of 20-40 ml/kg. A daily record is made of the animal's fluid and food intake. Body weights are recorded at least twice per week (daily during experiments). Health and hydration are assessed every day by both research and veterinary personnel. Water regulation is temporarily suspended if a monkey exhibits signs of dehydration (i.e. decreased urine production, dry feces, anorexia, changes in skin elasticity). These studies will provide information about the biological basis of memory in

healthy subjects, and suggest the means to modify and compensate for loss of memory function in stroke and brain trauma.

Species Used: Male rhesus monkeys (*Macaca mulatta*)
Number Used: 4

5. The following protocol involves an exception to the lighting and watering requirements for nonhuman primates. The exceptions were approved by the WFU ACUC, after determination of scientific justification.

A05-136: Neurophysiological Recording from Nonhuman Primate Brain
Full access to water is regulated in a manner to ensure animals are adequately motivated to perform traditional operant conditioning paradigms. Access to water is regulated such that the first fluid intake of the day will occur during a training or experimental session. A well-trained animal will work to satiety during an experimental session and, in doing so, obtain its minimum daily water requirement (as determined by a formula based on age, size and weight of the animal). In the event that the animal does not obtain its minimum fluid intake during a session, fluid is supplemented to the appropriate level when the animal is returned to its home cage. Typically, water regulation is begun on Sunday afternoon in preparation for behavioral testing on Monday. Animals participate in experiments on Monday through Friday and may receive additional water (or high-water-content fruit and vegetable supplements) on Friday afternoon through Sunday afternoon. Throughout the duration of an individual animal's participation in experimental protocols, fluid intake, body weight, behavioral performance, and observations of animal health are recorded daily. Periodic veterinary assessment, and other measures such as urine output, hematocrit, etc. are also used to assure the animals' continued health and well-being. Animals are weighed on the days they are tested (or at least weekly). Health and hydration are assessed every day by both research and veterinary personnel.

One of the aims of this study is to identify those brain areas most affected by brief (36-54 hour) sleep deprivation in an animal model. A monkey performs its behavioral/recording session normally during the day before sleep deprivation. That evening, before the lights go off in the housing area, the monkey is moved to a separate room in which the lights stay on all night and is kept awake by use of nonaversive stimuli (videos, music, food treats, toys, random computer sounds, interactions with technicians). The behavioral and electrophysiological testing of the monkey is then repeated the following afternoon. Sleep deprivation studies are performed at minimum 10 day intervals, typically only once per 2-4 weeks per monkey.

Species Used: Male rhesus monkeys (*Macaca mulatta*)
Number Used: 17

6. The following protocols involve exceptions to the lighting and space requirements for cats. The exceptions were approved by the WFU ACUC, after determination of scientific justification.

These studies examine the role of visual experience on the development of multisensory processes in the midbrain. From birth, kittens are raised to adulthood in total darkness. Total darkness is required to eliminate all visual experience during development in a reversible manner. Procedures such as enucleation or eyelid-suturing are inadequate because they are not reversible or allow a significant amount of light to penetrate the lids. A portion of the population is returned to full-spectrum lighting at six to twelve months of age. When in darkness, animals are cared for in accordance with all other standards and regulations. Infrared goggles are used by animal care, veterinary, and research personnel who enter the room daily to perform routine husbandry, health evaluations, and research manipulations. Criteria for monitoring the health and well-being of animals were developed, reviewed, and approved by the IACUC.

Animals in the room spend six hours per day together in an experimental pen which provides adequate space, but less than the minimum square footage per cat required by the USDA for standard housing. The size of the pen is a critical element in restricting the sensory experience of these animals, since it serves to constrain the minimum and maximum angular disparities of visual and auditory experience. Enlarging the size of the experimental pen would increase the maximal disparity beyond that which is believed to have an effect on reorganization in the nervous system. It is imperative that experimental animals are placed in the pen together to receive the same environmental manipulation. Any difference in the sensory experiences of the animals would constitute an unresolvable confound in the interpretation of the subsequently gathered data. It is important to note that animals are only in the run for six hours per day, after which they are returned to pens that provide the minimum square footage per cat required by the USDA. Results from this work are important for the improved treatment of children with visual disorders such as blindness, amblyopia, and strabismus.

A06-079: Development of Multisensory Integration
Species Used: Male and female domestic shorthair cats *(Felis domesticus)*
Number Used: 3

A07-117: Development of Multisensory Integration - Cats
Species Used: Male and female domestic shorthair cats *(Felis domesticus)*
Number Used: 2
A04-154 (2007 renewal pending): Experiential Influences on Cross-Modal Development
Species Used: Male and female domestic shorthair cats *(Felis domesticus)*
Number Used: 9

7. The following is an exception to requirements for ambient temperature requirements for nonhuman primates.

The macaque species that are currently housed in indoor/outdoor sheltered housing at the Friedberg campus are native to Southeast Asia or India. In their native countries, environmental temperatures are close to or above those recorded during the summer season in North Carolina, specifically average daily temperatures above 85^0F. Average daily temperature in the countries of origin of these species comparible or higher than North Carolina. These species are thus, tropical in nature, and have been acclimated to warm climates. In over 20 years of experience in housing macaque species in this environment and housing arrangement, we have not detected any clinical signs attributable to the high summer temperatures.

Temperatures are documented in the buildings each day and minimum and maximum temperatures recorded over each 24 hour period. Should the temperature of the indoor enclosure exceed 85^0F, the attending veterinarian or designee will assess the animals and ensure that the health and well-being of the monkeys is not at risk. The monkeys will be closely monitored for signs of heat exhaustion (lethargy, excessive water intake, dehydration, elevated respiratory rate, flushed appearance). The temperature and veterinary assessment will be documented and filed with the building temperature logs on any day that this occurs. In addition, auxiliary ventilation and cooling capacity in the form of large mobile fan units combined with water misters ("artic circles") will be provided on days when the ambient temperature is 85^0F or above.